

# The Golden Age of parasitology-1875–1925: the Scottish contributions

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## SUMMARY

The period 1875–1925 was remarkable in the history of parasitology partly because of the number of significant discoveries made, especially the elucidation of important life cycles, and partly because of the achievements of the clinicians and scientists who made these discoveries. What is remarkable is that so many of these individuals were Scots. Preeminent in this pantheon was Patrick Manson, who not only discovered the mosquito transmission of filarial worms but was instrumental in directly encouraging others to make significant discoveries in the fields of malaria, Guinea worm disease (dracunculiasis), onchocerciasis, loiasis and schistosomiasis and, indirectly, sleeping sickness and leishmaniasis. This chapter describes and discusses the contributions made by Douglas Argyll-Robertson, Donald Blacklock, David Bruce, David Cunningham, Robert Leiper, William Leishman, George Low, Patrick Manson, Muriel Robertson and Ronald Ross together with short biographical notes.

**Key words:** History, filariasis, onchocerciasis, loiasis, dracunculiasis, schistosomiasis, trypanosomiasis, leishmaniasis.

## INTRODUCTION

The term ‘Golden Age’ was first used by the Greek poet Hesiod (c.700 BC), a contemporary of Homer, who divided history into five ages of which the first was an idealized golden age of virtue. The term was later adopted by historians to refer to the period from about 500 to 300 BC when the Greek civilization flourished and has since been used with reference to many other civilizations to denote periods when humans lived in an ideal state of peace, harmony and stability. Gradually the term has taken on a wider meaning, periods when a particular art or activity was at its peak and has been applied to many sciences including astronomy, chemistry, physics and microbiology or sub periods within these broader periods. Most commentators on the history of science agree that these periods represent times when great tasks were accomplished to which I should like to add my own definition as ‘a period during which there was a concatenation of discoveries waiting to be made and the existence of individuals with the intellect and capability to make these discoveries’. Bacteriology is an excellent example. The golden age of medical bacteriology began with Louis Pasteur’s discovery of the anthrax bacillus in 1876 followed rapidly by the discovery of *Mycobacterium tuberculosis* and *Vibrio cholerae* and a host of other bacteria and microorganisms and the incrimination of these organisms in the causation of disease by

Robert Koch a decade later (Maloy and Schaecter, 2006; Blevins and Bronze, 2010). Thereafter the history of bacteriology has been mainly concerned with the discovery of new microorganisms and their association with disease.

There have been few attempts to define the golden age of parasitology. One of the rare mentions of the term is found in Morishita (1964) who recognized five periods of Japanese discoveries the fourth of which was ‘the golden age of Japanese parasitology’ from 1908 to 1945 characterized by the elaboration of the life cycles of important pathogens. There is a brief reference to the 19th century as the golden age of parasitology because this was a time when ‘many of the life cycles of parasites were elucidated and the various discoveries of previous centuries were pulled together into coherent stories’ (Cox, 2004) and there is a passing reference to the same period as ‘the golden years of tropical medicine’ by Bynum and Overy (1998) but no other serious attempts to define this golden age. It is therefore essential to go back to first principles. To celebrate its 100th issue in 1993, *Parasitology Today* (now *Trends in Parasitology*) published a list of 100 milestones in parasitology (Anonymous, 1993) and what is obvious from this list is that discoveries tended to come in clusters: a third between 1875 and 1925 and this is the period that I consider to be the golden age of parasitology for reasons that will be discussed later in this chapter.

Returning to the history of microbiology beginning in 1876 (coinciding with period with which we are now concerned) the important discoveries were the identification of bacteria and other

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microorganism and their role in the causation of disease. The history of parasitology is very different because by 1875 few of the medically important parasites had been discovered let alone associated with diseases. The gradual identification of important parasites and their association with diseases revealed yet further problems to be solved, how these parasites managed to get from host to host, in other words their life cycles. It is the unravelling of these life cycles that characterises this golden age of parasitology. The golden age defined by Morishita was also defined as the elaboration of life cycles but from a later Japanese perspective.

At the beginning of this chapter, I suggested that a golden age revolved around important discoveries waiting to be made and individuals capable of making these discoveries. What is remarkable in the field of parasitology, however, is that a disproportionate number of these discoveries were made by Scots. In order to understand these discoveries and the individuals involved during the golden age of parasitology it is necessary to consider the important diseases that were of most concern then and now. Selecting the important diseases is relatively easy. In 1975–1976 the World Health Organization established the Special Programme for Research and Training in Tropical Diseases and identified eight diseases that required special attention seven of which were caused by parasites: malaria, African trypanosomiasis (sleeping sickness), American trypanosomiasis (Chagas disease), schistosomiasis, lymphatic filariasis, onchocerciasis, visceral and cutaneous leishmaniasis (WHO, 1976). This chapter is concerned with all of these except Chagas disease. The important discoveries largely relating to understanding the biology and life cycles were made by a number of individuals but especially ten very talented Scots listed in Table 1 and it is their achievements that will be the subject of this chapter. It is worth noting that their achievements were recognized by their peers at the time, seven were Fellows of the Royal Society, four were knighted and five were Presidents of the Royal Society of Tropical Medicine and Hygiene.

#### THE SCOTTISH BACKGROUND

Before we consider these Scottish achievements it is necessary to understand the political and historical background of the time. Most historians agree that the foundations of the British Empire were first laid down during the reign of King Henry VII (ruled 1485–1509) when Britain, with its massive navy, began to establish trading and commercial links with far flung countries. There grew from these humble beginnings an empire that embraced the globe and, by 1830, Britain had become the predominant imperial and naval power in the world. In the last quarter of the 19th century the British

Empire consisted of dominions, colonies, protectorates, mandates and other territories with varying degrees of independence but all ruled and serviced from Britain. Such an immense empire had to be protected against invasion and local insurgences, which necessitated the presence of a large army which, in its turn, required a sophisticated system of medical services to enable the army to carry out its obligations. The prime concern of the British Government was to look after its soldiers thus the duties of the army medical officers were primarily to secure the health of the army, to look after the expatriate administrators and their families and, increasingly, the indigenous population as a whole.

The British army has had a long history of training doctors that began in the mid-17th century and gradually became more organized with the formation of the Army Medical Department after the Napoleonic wars in 1815, the Army Hospital Corps in 1857 and the Royal Army Medical Corps in 1898. In 1863 the army had established its own medical college at Netley, near Southampton, in Hampshire. Netley was to play a major role in the story of the great discoveries in tropical medicine and parasitology. This chapter will mainly be concerned with India, Uganda and China.

In India the predominant colonizing presence was the East India Company that had established a system of medical care in 1612–1614 and subsequently the Bengal Medical Service in 1764, the Madras Medical Service in 1767 and the Bombay Medical Service in 1779. These were merged to form the Indian Medical Service (IMS) in 1886 by which time the East India Company had ceded its domination of India to British rule together with responsibility for medical care. By then there were Army Medical Colleges and hospitals in Bombay (now Mumbai), Calcutta (Kolkata) and Madras (Chennai) the most important of which was Calcutta founded in 1835 and which trained doctors for work in the tropics.

Uganda was different from India in that it became a Protectorate in 1894. There had been a Church Missionary Society there since 1877 and this provided some degree of medical care. The country was of little interest to Britain and sometimes regarded as a ‘white elephant’. This all changed in the early 1890s when the country was ravaged with disease including rinderpest, smallpox and sleeping sickness and required urgent attention and the intervention of military doctors from Britain.

The third country of interest is China and the situation there was very different from that in India or Uganda. After the first ‘opium wars’ in 1842, Hong Kong was ceded to the British that in turn established five Treaty Ports in China: Shanghai, Canton (now Guangzhou), Foochow (Fuzhou), Ningpo (Ningbo) and Amoy (Xiamen). These were essential trading centres for goods between Britain and the Far East

Table 1. Ten Scottish scientists who made major contributions to tropical medicine and parasitology between 1875 and 1925.

Douglas Argyll-Roberston	1837–1909	Loiasis
David Breadalbane Blacklock	1879–1958	Onchocerciasis
Sir David Bruce FRS	1855–1932	African trypanosomiasis
David Cunningham FRS	1843–1914	Leishmaniasis
Robert Leiper FRS	1881–1969	Dracunculiasis, Schistosomiasis
Sir William Leishman FRS	1856–1926	Leishmaniasis
George Carmichael Low	1872–1952	Filariasis
Sir Patrick Manson FRS	1844–1922	Filariasis, Malaria, Loiasis., Onchocerciasis
Muriel Robertson FRS	1883–1973	African trypanosomiasis
Sir Ronald Ross FRS	1857–1932	Malaria, Leishmaniasis

and, as such, had to be protected and thus required a military presence which, in turn, required an efficient medical service.

From 1870 until 1875 the British Empire expanded rapidly in an unplanned way and towards the end of this period there arose problems at home due to the Long Depression in 1873–1879 exacerbated by the Irish famine of 1879. These factors, among others, led many professional people to seek a life in the Empire that was preferable to life in Britain and free from its suffocating class system. The various outposts of the Empire required administrators, lawyers, teachers, engineers and doctors and many of these were Scots. The reason for the dominance of Scots in running the Empire goes back to the 17th century when Scots attempted to establish their own empires in the Americas. In 1698, a fleet departed from Leith to Darien in Panama with the intention of establishing an empire there but this ambition was thwarted by their selection of a site, which happened to be one of the most malarious regions in the country. Unperturbed, later Scots tried to establish empires in the Americas, Africa and Asia, in all about fifteen, of which the names of some such as Nova Scotia and New Caledonia still reflect these enterprises but others, such as Scottish Guyana, Scottish Bengal, Scottish East India and Scottish India, which in the 1880s was the largest colony in Asia, are now lost in the mists of time.

It is against this background that the discoveries outlined in this chapter were made. Ambitious Scots doctors joined the Indian Medical Service or the Royal Army Medical Corps and were posted to distant parts of the Empire. Douglas Haynes has suggested that Scottish doctors were attracted to this kind of service because they often came from less wealthy families than their English counterparts and needed to find jobs quickly and, in any case, English doctors had tended to secure the better jobs in the UK (Haynes, 2001). Another factor was that with the emergence of Scottish Higher Education from the Enlightenment there was a spirit that engendered adventure and scientific knowledge. Whatever the reasons, Scottish doctors

found themselves in parts of the world ravaged by the old diseases cholera, smallpox, malaria, schistosomiasis and lymphatic filariasis and less familiar ones such as onchocerciasis, loiasis, sleeping sickness and leishmaniasis. For much of the time the duties imposed on Army doctors were not arduous so the more scientifically inclined had plenty of time to seek answers to some of the unsolved problems of tropical medicine and parasitology and to hand on the baton to later civilian workers. The achievements made between 1875 and 1925 were momentous as will be seen in the rest of this chapter.

Among these Scottish doctors serving in remote parts of the Empire one man dominated the field of parasitology and tropical medicine, Patrick Manson. Manson's discovery that filarial worms could be transmitted by mosquitoes in 1877 (see below) opened up the possibility that other parasites could also be transmitted by insects and doctors and scientists began to take up the challenge to solve what had been up to then the intractable problem of how parasites got from host to host. It seems sensible, therefore, to start this golden age of parasitology with this discovery but a more appropriate date might be 1875 when Manson, who had been working as a hospital surgeon in Amoy in China (now Xiamen then one of the so-called treaty ports effectively under British rule) returned to Britain where, in the reading room of the British Museum, he came across Timothy Lewis's 1872 account of worm-like parasites which he called *Filaria sanguinis hominis* (now *Wuchereria bancrofti*) in human blood and urine (Lewis, 1872). These discoveries transfixed Manson who acquired a new powerful microscope and returned to Amoy with the intention of looking for these parasites in his Chinese patients. From this inauspicious start, Manson was to make a number of pioneering discoveries that were to change the face of tropical medicine and parasitology for ever and would establish him as the 'Father of tropical medicine'. Manson had a remarkable knack of persuading clinicians, scientists and other influential people to support his various causes including filariasis, onchocerciasis, loiasis, dracunculiasis, schistosomiasis and malaria. Importantly, a number of the individuals that he recruited were

Scots and it is their achievements that are the subjects of this chapter, which is largely concerned with the establishment of life cycles and modes of transmission of parasites. The connections between Manson and these other scientists are shown in Fig. 1.

#### LYMPHATIC FILARIASIS

The discovery of the life cycle of filarial worms by Patrick Manson in 1877 is widely regarded as the most significant discovery in tropical medicine (Manson, 1878). Manson, first found larval stages, sheathed microfilariae, in the blood of dogs and humans infected with *Filaria sanguinis hominis* (later *Filarial nocturna* and now *Wuchereria bancrofti*) and noted that, on cooling, they emerged from their sheaths. He hypothesized that they might be transmitted by blood-sucking insects and that these might be fleas, bedbugs, lice, sandflies or mosquitoes. Here Manson's legendary 'luck' came into play; with little knowledge of entomology not only did he select mosquitoes as the most likely vectors but also chose the most susceptible vector species, the brown mosquito of Amoy, *Culex fatigans*. Manson tested his theory by feeding mosquitoes on the blood of his gardener, who was harbouring microfilariae (another stroke of 'luck'), and found developing larval stages in the mosquitoes, the first evidence that any pathogen could be transmitted by an arthropod vector. Manson's ideas were severely mocked at the time and were even described as representing 'either the work of a genius or, more likely, the emanations of a drunken Scots doctor in far off China where, as everyone was aware, they drank too much whisky' (Manson-Bahr, 1962). As for the mechanism of transmission, Manson was in little doubt that the parasites escaped from the mosquito into water and that humans became infected either by drinking this contaminated material or through the skin, theories based on his experience with the Guinea worm *Dracunculus medinensis*. The actual mechanism whereby mosquitoes transmitted filariasis was established later in 1899–1900 when the Australian parasitologist, Thomas Bancroft, sent fixed and embedded infected mosquitoes to Manson. Manson passed this material on to his colleague, George Carmichael Low, who prepared a series of beautifully prepared sections that clearly showed larval stages in the mouthparts of the mosquito (Low, 1900). Low was convinced that these were specialized forms awaiting an opportunity to enter a human when the mosquito next fed, which was also shown to be the case by Bancroft in 1899 (Bancroft, 1899).

Manson also became fascinated with the phenomenon of periodicity of microfilariae in the blood. This began with the casual observation that the boy he employed to examine blood at night recorded

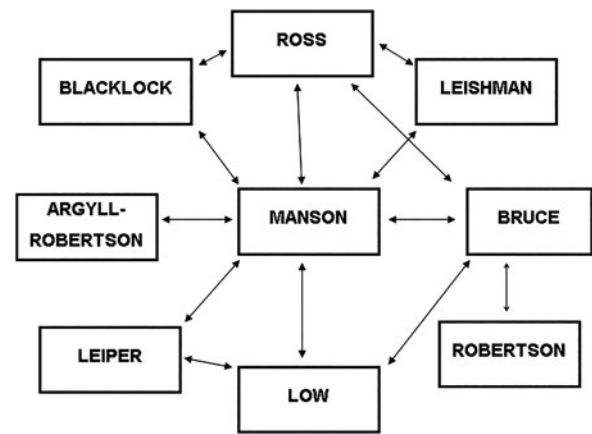


Fig. 1. Connections between Manson and other Scottish parasitologists in the period 1875–1925.

many more parasites than the one who worked during the day. This suggested to Manson that this was an adaptation that ensured that transmission occurred when the host mosquitoes were most active and he then showed that if an individual's sleep/wake pattern was reversed so was the periodicity (Manson, 1883). This was not only an interesting discovery in its own right but was later used to characterize infections caused by other filarial worms.

Manson's achievements are discussed more fully in Chernin (1983); Grove (1990); Eldridge (1992) and Manson-Bahr (1962).

#### LOIASIS

In 1890, an ophthalmologist, Stephen McKenzie, working at the London Hospital and a close friend of Manson, found some microfilariae in a patient from the Congo and, knowing Manson's interests, sent specimens to him for identification together with his case notes and asked for his opinion. Manson immediately became interested because these microfilariae were not familiar to him: they were from West Africa, their periodicity was diurnal and their sizes were different from those of *W. bancrofti*. Mackenzie provided Manson with further samples and after a number of false starts, mainly because some of these patients also, confusingly, harboured the microfilariae of what we now call *Mansonella perstans*, Manson concluded that there were at least two different kinds of microfilariae in humans, *Filaria sanguinis hominis* (*W. bancrofti*) that peaked at night and another that peaked during the day and that the latter were stages in the life cycle of *Loa loa* and probably transmitted by mosquitoes. In the event this turned out not to be the case and the vectors of loiasis, discovered by Robert Leiper in 1912, were actually flies of the genus *Chrysops* (Leiper, 1913). Understanding of the biology of *Loa loa* moved forward with the discovery of adult worms taken from the eye of a

patient by Argyll-Robertson in 1894–1895 who also, with Manson, described the male and female worms (Argyll-Robertson, 1895). Argyll-Robertson also made detailed studies of the clinical signs and pathology of loiasis and recorded the mysterious swellings known as Calabar swellings from which he extracted adult worms. With some foresightedness, Manson suggested that the pathology of loiasis might, in part, be caused by lymphatic obstruction (Manson, 1910).

#### ONCHOCERCIASIS

The microfilaria larval stages of *Onchocerca volvulus*, the causative agent of River Blindness, were first discovered by an Irish naval surgeon, John O’Neil, in skin snips from patients suffering from a skin condition known as *craw craw* in Ghana in 1874 (O’Neill, 1875). Some years later, in 1890, adult worms from a patient in Ghana were discovered by an unknown German doctor who sent specimens to Rudolf Leuckart in Leipzig who then forwarded them to Manson. Manson found that one of them was stuffed with larvae that were not those of *W. bancrofti* or *L. loa* and identified them as a new species, *Filaria volvulus* (a misprint for *volvulus* and now *Onchocerca volvulus*), unusually in a chapter in a text book, in which he did not mention O’Neill’s discovery nearly 20 years before (Manson, 1893). Manson believed that these worms might be transmitted by blood-sucking insects but did not follow this up. The actual role of blackflies, whose larvae live in streams and rivers, in the transmission of onchocerciasis was demonstrated by a Scottish professor, at the University of Liverpool, Donald Breadalbane Blacklock, then working in Sierra Leone in the mid-1920s (Blacklock, 1926). This discovery explained why this disease was known as river blindness and opened up the possibility of control by eliminating the blackfly larvae.

#### GUINEA WORM DISEASE, DRACUNCULIASIS

Manson also played a role in determining the life cycle of the Guinea worm, *Dracunculus medinensis*, one of the parasites described in the Bible and in the earliest literature. In 1819 Carl Rudolphi discovered that the adult female worms contained larvae and in 1836 Forbes found the larvae in water (See Grove, 1990). Over the next few years it was thought that humans became infected through the skin, as had been shown for hookworms and it was not until 1870 that the Russian scientist, Aleksej Pawlowich Fedchenko, began to investigate the possibility that small crustaceans belonging to the genus *Cyclops* might be involved in the life cycle and succeeded in infecting them with *Dracunculus* larvae (Fedchenko, 1870). He also suggested that humans

and other animals acquired their infections by accidentally consuming the infected crustaceans but was unsuccessful in his attempts to infect dogs. Fedchenko’s discoveries were controversial and remained so until they were confirmed by Manson in 1894. Manson, then working in London, acquired some worms from a patient and succeeded in infecting *Cyclops* from a local pond. Manson did not pursue this line of investigation but still maintained his interest in the subject and in 1905 persuaded his protégée, Robert Leiper, then working in the Gold Coast (Ghana) to carry on from where he had left off. Leiper repeated Manson’s (and Fedchenko’s) experiments and showed that when the infected crustaceans were exposed to acid they dissolved but the worm larvae remained alive (Leiper, 1906). Leiper suspected that this might be what happened in the human stomach and attempted to infect monkeys with infected crustaceans in banana leaves. At first he was unsuccessful but eventually he did succeed in infecting monkeys in this way. A number of later workers also failed to infect monkeys and it was not until 1913 that Dyneshvar Atmaran Turkhud successfully infected human volunteers with *Cyclops* containing the larval worms and later recovered the adults (Turkhud, 1913).

#### SCHISTOSOMIASIS

Manson also made important contributions to our understanding of human schistosomiasis, or bilharzia, an ancient disease now known to be caused by several species of *Schistosoma*, particularly *Schistosoma mansoni*, the intestinal form, *Schistosoma haematobium*, the urinary form, and *Schistosoma japonicum* the Asiatic form, but this was not known in the 1870s. The worm itself, in this case *S. haematobium*, was discovered by Theodor Bilharz in 1851 (Bilharz, 1853) and it was widely accepted that this species was responsible for both intestinal and urinary manifestations of the disease in Africa. In 1902 Manson, then working in London, found schistosome eggs in a patient who had lived in the West Indies and had never been to Africa. Manson realised the significance of this discovery that dispelled the belief that bilharziasis was an African disease and further speculated that molluscs or arthropods common to America and Africa might be the intermediate hosts. He also postulated that there were two species of *Schistosoma* in humans, one with eggs with lateral spines, responsible for the intestinal form of the disease, and the other, with terminal spines, the urinary form. This was not widely accepted at the time but Manson would not be put off and persuaded Leiper to look into this problem. Leiper made several trips to schistosomiasis endemic areas, the first to Egypt in 1906 and later

in 1915 where on both occasions he worked with the eminent German helminthologist, Arthur Looss and together they began to work out how schistosomes were transmitted but were unsuccessful. Looss had already identified over 50 species of freshwater snails as possible intermediate hosts but this potentially fruitful collaboration was abandoned at the outbreak of the First World War when Looss, as a German, was forced to leave Egypt. In 1914 Leiper firmly established the existence of *S. mansoni* as a species distinct from Bilharz's worm; *S. haematobium*.

The search for the intermediate stages in the life cycle of schistosomes took a long time and a number of experienced parasitologists, including Arthur Looss, Prospero Sonsino and Thomas Cobbold, working at the end of the 19th century, all failed to infect snails with schistosome larvae and it was not until 1915 that Leiper demonstrated the complete life cycle in their snail hosts. At about the same time he established that the two species that he had differentiated had different intermediate hosts: the terminal-spined egg, *S. haematobium*, transmitted by snails of the genus *Bulinus* and the lateral-spined egg, *S. mansoni*, by snails of the genus *Planorbis* (*Biomphalaria*) (Leiper, 1916). The nomenclature of the snail hosts has subsequently been changed. The third important species, *S. japonicum*, had been discovered by Fujiro Katsurada in 1904 and its development in the snail host described by Miyairi and Suzuki (Miyairi and Suzuki, 1913) 2 years before Leiper independently described the life cycle of *S. haematobium*. Unfortunately the Japanese workers published their findings in Japanese journals that were not available outside Japan and Leiper was unaware of their findings until he had made his own discoveries.

A summary of the helminthological discoveries made by Scottish parasitologists is given in Table 2.

#### MALARIA

Probably Manson's best known and most important contribution to science and medicine was his role in the discovery that malaria was transmitted by mosquitoes. Malaria parasites had been seen for the first time by the French physician, Charles Alphonso Laveran in 1880 (Laveran, 1880) but very little was known about the possible mode of transmission of malaria except that it was associated with swamps and that these were ideal habitats for mosquitoes; Laveran had actually suggested that mosquitoes might be the vectors. Manson, working in London and having already established the principle of vector transmission of diseases with filarial worms and mosquitoes turned his attention to malaria and hypothesized that part of the life cycle of the malaria parasite must occur outside the human body in another host, probably a mosquito

(Manson, 1894). Manson, however, had no access to malaria patients under natural conditions or possible mosquito hosts but in 1894 he recruited the help of an unlikely colleague, Ronald Ross a young army surgeon then working in malarious areas in India and on leave in London. Manson worked on Ross's initial reservations and directed operations at a distance. Ross, like Manson, believed that humans became infected through drinking water in which mosquitoes had laid their eggs and had actually tried to infect some local inhabitants with such water. Ross then began a series of definitive studies in which he fed mosquitoes on the blood of infected individuals and, sensibly, selected those mosquitoes that were locally most common. Unfortunately for Ross these were culicine mosquitoes that do not transmit malaria. Nevertheless, he eventually turned his attention to less common dappled-winged mosquitoes, now known to be *Anopheles* spp., and succeeded in infecting them. By 1895, he was on the brink of demonstrating that anopheline mosquitoes could transmit human malaria but was unable to complete his studies because at this crucial stage he was posted to Bangalore to investigate an outbreak of cholera and later to Calcutta where there was very little malaria. In Calcutta, he did have access to laboratory facilities and, on Manson's advice, he turned his attention to malaria parasites of birds and after, a number of setbacks hit on the right combination of a malaria parasite, *Plasmodium relictum* that could be transmitted by culicine mosquitoes. Ross demonstrated that mosquitoes fed on infected birds infected new hosts when the infected mosquito fed again (Ross, 1897). These experiments finally convinced Manson, that malaria was transmitted through the bite of a mosquito, contrary to his earlier opinion that the infective stages were discharged into water.

Ross surmised correctly that human malaria was probably transmitted in the same way but the actual proof still remained unresolved. Ross recorded that one single experiment could bring about the life cycle of human malaria but his military duties took precedence and he was sent to work on an epidemic of plague that was then spreading across India and was not allowed to test his hypothesis because of the plague (See Nye and Gibson, 1997).

In the meantime in 1898 the Italian workers, Guiseppe Bastianelli, Amico Bignami and Giovanni Battista Grassi produced the final proof of transmission of malaria to humans by mosquitoes when they fed local *Anopheles* mosquitoes on infected patients and subsequently transmitted the infection to uninfected individuals via the bite of these mosquitoes. (Bastianelli *et al.* 1898; Bastianelli and Bignami, 1900). It is now generally, but not universally, agreed that Ross's contribution to our knowledge of malaria was that he was the first person to establish the whole of the life cycle

Table 2. Key discoveries by Scottish parasitologists in the field of helminthology.

1877	Manson demonstrates mosquito transmission of <i>Wuchereria bancrofti</i>
1879	Manson describes periodicity in <i>W. bancrofti</i> filariasis
1890	Manson recognises <i>Loa loa</i> microfilariae
1891	Manson distinguishes between <i>W. bancrofti</i> and <i>L. loa</i> microfilariae and their periodicities
1891	Manson predicts that <i>L. loa</i> is transmitted by a blood-sucking insect with day-biting habits
1893	Manson describes <i>Onchocerca volvulus</i> adult worms
1894	Manson confirms Fedchenko's observation that <i>O. volvulus</i> larvae develop in the crustacean <i>Cyclops</i>
1895	Argyll-Robertson removes <i>L. loa</i> worm from eye of patient
1895	Argyll-Robertson and Manson describe adult <i>Loa loa</i>
1900	Low demonstrates <i>Wuchereria bancrofti</i> larvae in mosquito proboscis
1906	Leiper implicates <i>Cyclops</i> in the transmission of <i>Dracunculus medinensis</i>
1910	Low distinguishes between <i>L. loa</i> and <i>W. bancrofti</i> microfilariae.
1912	Leiper discovers that <i>Loa loa</i> microfilariae develop in <i>Chrysops</i> flies
1914	Leiper implicates snails in the transmission of schistosomes
1916	Leiper differentiates between <i>Schistosoma mansoni</i> and <i>S. haematobium</i>
1923	Low describes the relationship between <i>Loa loa</i> and Calabar swellings
1925	Blacklock describes development of <i>O. volvulus</i> microfilariae in blackflies

of malaria parasites in birds and mosquitoes and that it was the Italian workers who first demonstrated the whole life cycle in anopheline mosquitoes and humans. In 1902 Ross was awarded the Nobel Prize for Physiology or Medicine much to the annoyance of the Italian workers with whom Ross never established any rapport. Both Manson and Laveran were nominated for the 1902 Nobel Prize and Laveran was so honoured in 1909. Manson was never awarded the Nobel Prize that he so richly deserved. Ross's association with Manson also became very acrimonious in later years (Bynum and Overy, 1998).

The life cycle in humans, however, remained incompletely understood and nobody knew where the parasites developed during the first 10 days or so after infection during which they could not be seen in the blood. A number of workers became convinced that there must be a stage outside the blood cells in the life cycle of the malaria parasites but what form this took was not known. This question was not resolved until 1947 when another Scot, Henry Shortt, together with Cyril Garnham, working in London, first with chimpanzees and then with human volunteers, showed that a phase of division in the liver preceded the development of parasites in the blood—now known as the exoerythrocytic stage to distinguish it from the erythrocytic stage in the blood (Shortt and Garnham, 1948; Garnham, 1966).

#### AFRICAN TRYPANOSOMIASIS

African trypanosomiasis, sleeping sickness in humans and a wasting disease, nagana, in cattle are ancient diseases but their causes and mode of transmission remained unknown until the second half of the 19th century. In 1857, David Livingstone began to suspect that nagana might be transmitted by tsetse flies but he had neither the experience nor

the facilities to elaborate on this and it was not until over 35 years later that the scientific understanding of African trypanosomiasis began. In 1894, David Bruce, a Scot then working as a British Colonial Medical Officer, was sent to South Africa to investigate an outbreak of nagana as it was known by the local people and 'fly disease' by hunters and travellers. Bruce, a bacteriologist, had worked with the eminent German bacteriologist Robert Koch and in 1884 had identified the bacterium *Brucella* as the cause of Malta fever now known as brucellosis in his honour. Bruce, who had expected to incriminate bacteria as the cause of nagana, found organisms in the blood of diseased cattle that resembled the trypanosome (*Trypanosoma evansi*) that Evans had found in horses and other animals suffering from surra, a disease similar to nagana, in India a few years earlier (Evans, 1881). Bruce surmised that these trypanosomes, now known to be *Trypanosoma brucei brucei*, were the cause of 'fly disease' and demonstrated that inoculating infected blood into uninfected cattle, horses and dogs caused nagana (Bruce, 1895). Bruce was a keen observer and noted that infected cattle had spent some time in the fly infested 'tsetse belt' and suggested that tsetse flies might act as vectors of the disease. Bruce then sent uninfected cattle and dogs into the 'fly country' and when they returned they were found to be infected with trypanosomes. It was some time before he conclusively demonstrated that indeed trypanosomes were transmitted by tsetse flies but thought that transmission was purely mechanical (See Bruce, 1915).

By 1884–1885, Bruce had conclusively demonstrated that the cattle disease, nagana, was caused by trypanosomes transmitted by tsetse flies. He had not, however, associated these discoveries with sleeping sickness in humans although Manson had written to him in 1896 suggesting that sleeping sickness might be similar to nagana and, in 1897, that the

disease might be transmitted by tsetse flies. In 1900 Manson saw organisms that were certainly trypanosomes in the blood of a patient suffering from sleeping sickness but was unable to obtain another blood sample. The next important step was in 1901 when a British Colonial surgeon, Robert Michael Forde, found organisms that he first thought were worms in the blood of an English patient in the Gambia. He showed these to Joseph Everett Dutton who realised that they were trypanosomes which he named *Trypanosoma gambiense* (now *Trypanosoma brucei gambiense*) now known to be the causative organism of Gambian or chronic sleeping sickness (Dutton, 1902). Manson was still pursuing his interest in sleeping sickness and in 1902 he conclusively identified trypanosomes in a patient recently returned from the Congo.

In the meantime, in 1902, the British Foreign Office requested the Royal Society to set up a Sleeping Sickness Commission to investigate the problem of a wasting disease of humans in Uganda. The Commission, consisting of a Scot, George Carmichael Low, Cuthbert Christy and a young Italian, Aldo Castellani, concluded that, despite Manson's suggestion, the disease was caused by a streptococcus and a paper to this effect was submitted to the *Proceedings of the Royal Society* by Castellani. Its publication was blocked by David Bruce who was unconvinced by the data presented. It is also possible that Bruce and the Foreign Office were concerned that should sleeping sickness be caused by a bacterium it would be necessary to develop a vaccine at considerable expense. The Royal Society then sent out a second Commission consisting of Bruce, Aldo Castellani and David Nabarro in 1903. At some point Castellani changed his mind about a bacterial cause and started to believe that trypanosomes were the cause of the disease. A controversy then arose between those that argued that Bruce had discovered that human sleeping sickness was caused by trypanosomes or that Castellani did. It is quite possible that the truth lies somewhere between these extremes and that Castellani began to suspect that trypanosomes were involved only when he learned that Bruce was being sent to Uganda or that Bruce inadvertently provided him with some clues. Moving on, we do know is that by 1910 Bruce thought that that all forms of sleeping sickness were caused by infection with *T. b. gambiense*, This was to be challenged with the discovery of another 'species' *T. rhodesiense* (now *T. b. rhodesiense*) by John William Watson Stephens and Harold Benjamin Fantham in 1910 that could also infect cattle and game animals (Stephens and Fantham, 1910). So by 1910, Bruce had come to the conclusion that *T. b. rhodesiense* and *T. b. brucei*, the trypanosome responsible for nagana, were the same, that sleeping sickness was a human form of nagana and that infected wild (and

domesticated) animals must serve as reservoir hosts (Bruce, 1915). This belief was only slightly modified by subsequent discoveries and it became clear that there were two distinct forms of human sleeping sickness in Africa, a chronic form caused by *T. b. gambiense* transmitted by *G. palpalis*, mainly in riverine conditions in Central and West Africa, and an acute form caused by *T. b. rhodesiense* transmitted by *G. morsitans* in the East African savanna and capable of infecting game and cattle and that, there was also a third species, *T. b. brucei*, a parasite of cattle and game that did not infect humans (See Hoare, 1972).

The actual life cycle of the African trypanosomes remained controversial until Friedrich Kleine, a colleague of Robert Koch, demonstrated cyclical transmission but mistakenly thought that there was an obligatory sexual stage in the life cycle. This error was not surprising because trypanosomes in the blood occur in two forms, short stumpy and long thin. It is now known that *T. b. brucei* can undergo sexual reproduction in the tsetse fly: *T. b. gambiense*, on the other hand, appears to have abandoned sex and the population is therefore clonal. Bruce and another Scot, Muriel Robertson, both working in London, were intrigued by this phenomenon and subscribed to the two sex hypothesis and suggested that the slender forms were the males and the stumpy forms the females. Robertson soon realized that the two forms were actually successive stages in the same life cycle and that only the slender forms were able to divide and surmised that the stumpy forms were the stages infective to tsetse flies and abandoned her earlier theory. Armed with this knowledge, Robertson began a meticulous study of the fate of *Trypanosoma congolense*, a parasite of cattle also belonging to the same salivarian group as *T. brucei*. *Trypanosoma congolense* is able to complete its development in several species of *Glossina* and Robertson had ample material at her disposal and her 1913 detailed descriptions of the development of trypanosomes from being taken up from the blood to the infective stages in the tsetse proboscis including their circuitous route via the endoperitrophic space remains essentially the same today (Robertson, 1913). Whereas Robertson used *T. congolense* in her studies. Bruce, at about the same time, had described the developmental cycle including the migration of the *T. b. rhodesiense* to the salivary glands of tsetse flies in 1914 (Bruce, 1915). Bruce was fulsome in his praise for Robertson and in 1914 remarked that 'she has done some of the best work in this branch of protozoology' (Hoare, 1972).

In his 1895 report Bruce had noted that the trypanosomes in the blood of cattle persisted for some time and that the numbers of parasites in the blood fluctuated considerably over time. This phenomenon was subsequently recorded by several authors



including Ronald Ross and David Thomson who, 1911, published charts of the fluctuating parasitaemia in humans having followed a single case for 73 days (Ross and Thompson, 1911). In passing, it is worth mentioning that their chart has been used by virtually every author or speaker on the subject of antigenic variation ever since partly because of its clarity and simplicity (see below). Bruce was unable to follow up his initial observations but in 1905 one of Ehrlich's colleagues, Ewald Franke, suggested that the reason why trypanosomes persisted in the blood was that they had become resistant to antibodies. In 1907, Aldo Massaglia argued that the fluctuating waves of parasites in the blood could be explained if most trypanosomes were killed by antibodies in the blood but a few were able to survive and give rise to the next wave (Massaglia, 1907).

These observations were largely ignored until 1912 when Muriel Robertson began to look at the problem again. Robertson followed up her earlier observations that there were two forms of trypanosomes in the blood, long slender forms that divided and short stumpy forms that did not and were infective to tsetse flies. She noted that the first forms that appeared in the blood were the long slender dividing forms and that they appeared as waves in the blood, sometimes completely disappearing, and postulated that there was a tension between the capacity of the host to destroy the parasite and the capacity of the parasite to maintain itself (Robertson, 1912). Robertson got tantalisingly close to establishing that it was the immune response that was responsible for the fluctuating parasitaemias and commented on 'liberation in the serum of protective substances' an idea not so different from those put forward by Massaglia in 1907. However, the facilities to pursue this further were not available at that time. Subsequently with the availability of the electron microscope and new cytological techniques, it gradually became clear that the basis of antigenic variation lay in the trypanosome itself and the fact that it was the protein coat that was the variant antigen was discovered by Keith Vickerman later Regius Professor of Zoology in the University of Glasgow in the 1960s (Vickerman and Luckins, 1969).

#### LEISHMANIASIS

Old World leishmaniasis occurs in two principle forms, cutaneous and visceral (Kala Azar) both with a variety of manifestations and local names. The organisms causing Old World cutaneous leishmaniasis were described independently by the Scot, David Cunningham, who described 'peculiar parasitic organisms' in macrophages from a case of Delhi boil in 1885 in a brief paper that has long been neglected (Cunningham, 1885) and also by

the Russian, Peter Fokish Borovosky (Borovsky, 1898) and, independently, by the American James Homer Wright and named by him *Leishmania tropica* (Wright, 1903). There are no good records of visceral leishmaniasis until early in the 19th century when military physicians began to record outbreaks of a novel febrile disease, black disease or Burdwan fever, in Bengal and with local names such as Dumdum fever from other parts of India. Its cause was unknown and was sought by eminent experts in tropical medicine including Ronald Ross and Leonard Rogers both of whom thought that it was a form of malaria. In 1900 William Boog Leishman, then working at the Army Military College at Netley, found the parasites in spleen cells from a soldier who had been serving in India and was suffering from Dumdum fever. Over the next few years, Leishman found these organisms in a number of other cases but did not pursue these findings at the time. Two years later, when he was working with *Trypanosoma brucei* in rats, he noticed that degenerating trypanosomes resembled the organisms he had seen earlier in the spleen of his Dumdum patient (Leishman, 1903). Basing his finding on the earlier work of Bruce and others on trypanosomes, he correctly assumed that the parasites he saw were similar to trypanosomes and sent his material to Ross who realized that they were not trypanosomes but novel organisms, which he named *Leishmania donovani* (Ross, 1903). In the same year, Charles Donovan, another army physician serving in India, independently described similar parasites from a patient suffering from Dumdum fever in Madras (Donovan, 1903). Donovan sent his specimens to the French protozoologists, Alphonse Laveran and Félix Mesnil, who at first thought that they were piroplasms, an error soon corrected by Ross who also sorted out the question of priorities. The names of Leishman and Donovan are now commemorated in the popular designation of the intracellular parasites as Leishman-Donovan, or LD, bodies. In passing it is worth mentioning that Borovsky's discoveries, published in Russian, were not known to Leishman or Donovan. It was some years before the role of sandflies in the transmission of leishmaniasis was discovered (Sergent *et al.* 1921).

Although Leishman is recognized for his discovery of the organisms responsible for Kala Azar he is much better known for his development of a blood stain that now bears his name. Leishman's stain belongs to the Romanowsky stain group based on ripened methylene blue and eosin and which had the advantage of fixing blood smears as well as staining them. Leishman's stain colours nuclear material a dark red purple and is widely used in haematology. Its value in the field of parasitology is that it is particularly useful for staining malaria parasites, trypanosomes and leishmanial

Table 3. Key discoveries by Scottish parasitologists in the field of protozoology.

1885	Cunningham describes leishmanial parasites from a case of cutaneous leishmaniasis (Delhi boil)
1894	Bruce sees trypanosomes in the blood of cattle suffering from nagana and suggests transmission by tsetse flies
1894	Manson develops theory of mosquito transmission of malaria
1897	Ross demonstrates transmission of avian malaria parasites by mosquitoes
1900	Manson demonstrates transmission of human malaria by mosquitoes
1902	Bruce finds trypanosomes in cerebrospinal fluid of sleeping sickness victim
1903	Leishman and Donovan independently describe leishmanial parasites in cases of visceral leishmaniasis (Kala Azar)
1903	Bruce shows that trypanosomes are the cause of sleeping sickness and are transmitted by tsetse flies
1911	Bruce observes development of trypanosomes in tsetse flies
1915	Robertson describes development of trypanosomes in tsetse flies and suggests that antibodies might be involved in fluctuating parasitaemias

parasites. The use of this stain for the rapid and accurate identification of parasites has been a major contributor to the diagnosis and control of parasitic diseases.

#### THE WIDER WORLD OF PARASITOLOGY

By its very nature this chapter that has been concerned with the achievements of Scottish parasitologists has had to be very selective but their work was not carried out in isolation from the contributions made by non-Scottish contemporaries and their predecessors. For those interested in the histories of parasitology and tropical medicine there is a very rich literature concerning the period prior to 1875 and subsequent discoveries. The classic text is *A History of Parasitology* by W.D Foster that includes chapters on schistosomiasis, lymphatic filariasis, Guinea worm, trypanosomiasis and malaria (Foster, 1965). Other comprehensive books include *The Wellcome Trust Illustrated History of Tropical Diseases*, in which each chapter is written by a practicing exponent, covers these diseases and also, *inter alia*, onchocerciasis (Cox, 1996) and *Parasites and Parasitic Infections in early Science and Medicine* (Hoepli, 1959). There are also useful reviews including Chernin, 1983 and Cox, 2002). Helminth infections are particularly well served in Grove's scholarly *A History of Human Helminthology* (Grove, 1990). There is nothing comparable in the field of protozoology but Wenyon's two volume classic, *Protozoology: A Manual for Medical Men, Veterinarians and Zoologists*, which, although not a historical book, has a vast amount of information about malaria, African trypanosomiasis and leishmaniasis (Wenyon, 1926). Individual diseases are well served in the literature (See, Cox, 2002, 2004, Warboys, 1993) (Table 3).

#### SHORT BIOGRAPHIES

##### *Douglas Moray Cooper Lamb Argyll-Robertson 1837–1909*

Douglas Argyll-Robertson was born in Edinburgh in 1837 and educated at the Universities of St Andrews,

Berlin and Edinburgh where in 1857 he graduated in Medicine. He later specialized in ophthalmology having studied in Prague under von Arlt and in Germany under von Graefe. Appointments included assistant ophthalmic surgeon at the Edinburgh Royal Infirmary in 1867 and ophthalmic surgeon in 1870. In 1895 he found adult *Loa loa* worms in a patient who had been resident in Old Calabar, Nigeria and sent them to Manson and together they published the first detailed accounts of the male and female worms. In the same year he described the successful extraction of the adult worm from the eye of a patient. Argyll-Robertson continued to study the disease caused by *Loa loa* and published detailed accounts of the pathology and also described Calabar swelling from which he extracted a worm. He retired in 1904 and died suddenly on a visit to Gondal, India in January 1909. For more information see Power, 2004.

##### *Donald Breadalbane Blacklock 1879–1955*

Donald Blacklock was born in Oban, Argyllshire, in 1879 and educated at the University of Edinburgh where he graduated in Medicine and Surgery in 1902. After practicing medicine in South Africa he studied tropical medicine in London and Liverpool and in 1911 was appointed Research Assistant at the Liverpool School of Tropical Medicine and later, in 1914, Lecturer in Parasitology during which time he worked mainly on trypanosomiasis. During the First World War he served in the Royal Army Medical Corps. In 1921 he was appointed Professor of the Tropical Diseases of Africa and Director of the Sir Alfred Lewis Jones Research Laboratory in Freetown, Sierra Leone. While working in Sierra Leone in 1923 he turned his attention to the problem of onchocerciasis and established that the blackfly, *Simulium damnosum* was the vector of *Onchocerca volvulus* and published his findings in 1926. During his time in Sierra Leone working with John Gordon Thompson they infected *Physopsis* snails with *Schistosoma haematobium*, collected the cercariae and infected monkeys and guinea pigs. On his return to England he was appointed Professor of Parasitology in Liverpool and later Professor of

Tropical Hygiene in 1934. During the Second World War, he served as Surgeon-Captain in the Royal Navy Volunteer Reserve again in Sierra Leone where he was involved in implementing anti-malaria control measures. He died in Cornwall in 1955. For more information see Grove, 1990.

#### *Sir David Bruce 1855–1931*

David Bruce was born in Melbourne, Australia, the son of Scottish parents from Edinburgh. At the age of 5 he came to live in Stirling and, in 1876, enrolled in the University of Edinburgh to read Zoology but switched to Medicine and graduated Bachelor of Medicine and Surgery in 1881. Shortly after graduating he joined the Army Medical Service as a bacteriologist and was posted to Malta to investigate a disease of humans, Malta fever. He quickly identified the bacterial cause of the disease now named after him, brucellosis, *Brucella melitensis*. In 1894 Bruce was sent to South Africa to investigate the cause of a serious wasting disease of cattle, nagana. He found trypanosomes in the blood of infected cattle and in 1896 demonstrated that they were transmitted by tsetse flies, *Glossina* spp. In 1899 he was appointed Professor of Pathology at the Royal Victoria Medical College at Netley. In 1901, Bruce was sent, with Aldo Castellani, as a member of the Royal Society Sleeping Sickness Commission, to investigate an epidemic of human sleeping sickness that was sweeping across Uganda. Bruce initially suspected that the cause was bacterial but found trypanosomes in the blood of victims and in 1903 established that these were the actual cause of sleeping sickness and that they were transmitted by tsetse flies. The controversy regarding priority between Bruce and Castellani rolled on for years with ill feeling on both sides. In 1914 he was appointed Commandant of the Royal Medical College at Milbank in London and retired in 1919. Bruce was the recipient of many awards and prizes including Fellowship of the Royal Society in 1899 and Knight Commander of the Honourable Company of the Order of the Bath (KCB) in 1918. David Bruce always worked very closely with his wife and died 4 days after her while attending her memorial service in London in 1931. For more information see Hamerton, 1931 and Christophers, 2004.

#### *David Douglas Cunningham 1845–1914*

David Cunningham was born in Prestonpans, east of Edinburgh and educated at the Royal College of Physicians of Edinburgh and the University of Edinburgh where he graduated in Medicine in 1867. In 1868 he joined the Indian Medical Service and was posted to Calcutta where there was an epidemic of cholera. In 1879 he was appointed Professor in the Calcutta Medical College. Cunningham's main

interests were cholera and the study of airborne fungal spores and when, in 1885, he discovered spherical bodies in samples taken from a patient suffering from Delhi boil. He assumed that they were fungal spores but did not pursue this observation any further. It was not until 1903 when Leishman discovered similar bodies in patients with Kala Azar that the leishmanial significance of his discovery was realised. In 1888 he was appointed Surgeon Major to the Bengal Medical Service and Honorary Surgeon to the Viceroy of India. He was elected Fellow of the Royal Society in 1889 and Companion of the Order of the Indian Empire in 1893. He retired early due to ill health in 1896 but in 1898 he was appointed Honorary Physician to King George V. He died in Torquay in 1914. For more information see D.P. 1971 and Chandra and Coulton, 1999.

#### *Robert Thompson Leiper 1881–1969*

Robert Leiper was born in Kilmarnock in 1881 and educated initially at the University of Birmingham and then at the University of Glasgow where he graduated in Science, Medicine and Surgery in 1905. On graduation he joined the staff at the London School of Tropical Medicine where he founded the Department of Helminthology. In the same year he worked with the German helminthologist, Arthur Looss on the problem of schistosomiasis in Egypt and later worked in Nigeria in 1912 and China and Japan in 1914. During the Second World War he served with the Royal Army Medical Corps in Egypt. Leiper's most important achievements included the incrimination of *Bulinus* snails in the transmission of *Schistosoma haematobium* and *Biomphalaria* snails in the transmission of *S. mansoni*, the involvement of the crustacean *Cyclops* in the life cycle of *Dracunculus medinensis* and the incrimination of *Chrysops* flies in the transmission of *Loa loa*. He also made important contributions to our knowledge of the life cycles of the flukes *Clonorchis sinensis*, *Metagonimus yokogawa*, *Opisthorchis viverrini* and *Echinostoma malayanum*. In 1924, Leiper was appointed Professor of Helminthology at the London School of Hygiene and Tropical Medicine, a position he held until he retired from full-time work in 1946. He founded the *Journal of Helminthology* and *Helminthological Abstracts*. Among numerous honours, he was elected Fellow of the Royal Society in 1921 and was made a Companion of the Order of St Michael and St George (CMG) in 1941. Leiper died in Hertfordshire in 1969. For more information see Garnham, 1970 and Farley, 2004.

#### *William Boog Leishman 1865–1926*

William Leishman was born in Glasgow and educated at the University of Glasgow where he

graduated in Medicine in 1886. He then joined the army and was posted to the Royal Army Medical School in India as surgeon to the medical staff. In 1897 he returned to UK as Assistant Director of Pathology at the Royal Army Medical College at Netley. When the College moved from Netley to Millbank in London in 1903, Leishman succeeded Almoth Wright as Professor of Pathology. While working in India, Leishman became interested in Kala Azar, also known as Dumdum fever, and believed, as did many others, that this disease was a manifestation of malaria. In 1901 while examining blood slides for malaria he observed small oval bodies that he thought might be degenerating trypanosomes but did not pursue this matter further until 1903 when he showed his slides to Ronald Ross who realised what they were and named them *Leishmania donovani*. While working at Netley, Leishman developed a new stain for blood slides consisting of ripened methylene blue and eosin and which stained nuclei dark red purple. This stain proved to be particularly good at staining blood parasites including malaria parasites and trypanosomes and is still used today. In 1913, Leishman took up a post as Expert in Tropical Diseases to the Army Advisory Board. During the First World War, Leishman fought successfully to have Allied soldiers immunized against tetanus and thus saved thousands of lives. In 1918 he was recalled to the War Office as Director of Pathology and in 1923 was appointed Director General of Army Medical Services. Leishman was the recipient of many honours including a knighthood in 1909, Fellowship of the Royal Society in 1910, Knight Commander of the Order of St Michael and St George (KCMG) in 1918 and Knight Commander of the Honourable Order of the Bath (KCB) in 1924 and was also awarded the French Legion d'Honneur and the US Distinguished Service Medal. Leishman died in London in 1926. For more information see Rolleston, 2004.

#### *George Carmichael Low 1872–1952*

George Low was born in Monifieth, Forfarshire, in 1872 and educated at St Andrews University and later at the University of Edinburgh where he graduated in Medicine in 1897. From 1897 until 1899 he worked as a hospital doctor at the Royal Infirmary in Edinburgh. In 1899 he left Edinburgh for London where he studied under Manson at the London School of Tropical Medicine, then at the Albert Dock, and became his research assistant. In 1899, he was sent by Manson to Heidelberg to learn the most recent histological techniques, which served him well when, in 1900, the Australian helminthologist, Thomas Lane Bancroft, sent Manson some preserved mosquitoes infected with *Wuchereria bancrofti*, which low sectioned and traced the

development of larval worms to the mouthparts of the mosquito thus completing our knowledge of the life cycle and mode of transmission of filarial worms. In 1900 he spent 3 months in a highly malarious area in the Roman Campagna where he participated in an experiment that showed that sleeping in a mosquito-proofed hut protected the inhabitants against malaria. In 1901, he travelled to the Caribbean, where he worked on filariasis and, in 1903 he was a member of the unsuccessful Royal Society Commission sent to investigate the cause of sleeping sickness in Uganda. He never travelled to the tropics again and spent the rest of his career at the London School of Tropical Medicine, first at the Albert Dock and later at Endsleigh Gardens in London, where he became Director of Clinical Tropical Medicine and worked on various aspects of filariasis, schistosomiasis, malaria and leishmaniasis. Together with Sir James Cantlie, another Scot and Aberdeen graduate, he founded the Royal Society of Tropical Medicine and Hygiene in 1907. Low was also Physician in Ordinary to King George V. Low died in London in 1952.

For more information see Cook, 1993 and Warboys, 2004.

#### *Sir Patrick Manson 1844–1922*

Patrick Manson was born in Oldmeldrum, Aberdeenshire in 1844 and educated at the University of Aberdeen where he graduated in Medicine and Surgery in 1865. He spent a short time as assistant medical officer at the Durham Lunatic Asylum before joining the Chinese Maritime Customs in Formosa (now Taiwan). In 1875 he was posted to Amoy in China where he became interested in lymphatic filariasis and in 1877 established that the parasite, now known as *Wuchereria bancrofti*, was transmitted by mosquitoes. In 1883 he moved to Hong Kong where he was instrumental in the foundation of the Hong Kong College of Medicine for the Chinese and was its Dean in 1887. Manson returned to England in 1889 and set up a medical practice in London and constructed a laboratory in his own house. He was appointed physician to the Albert Dock Hospital in 1892 and medical adviser to the Colonial Office in 1894. Although working in London, Manson had access to a plentiful supply of clinical material from patients who had returned from the tropics and in 1891 discovered the microfilariae of *Loa loa* and, with Argyll-Robertson, he described the adult *Loa loa* worms in 1895. Manson had a knack of encouraging other workers and was able to develop a number of collaborations with scientists and clinicians. In 1894, he persuaded Ronald Ross, then working in India, to investigate the role of mosquitoes in the transmission of malaria and who worked out the whole life cycle in 1897. Manson also

developed fruitful working relationships with other collaborators including Robert Leiper working with schistosomes, loiasis and Guinea worm and George Carmichael Low working with filarial worms and was in correspondence with, and shared ideas on sleeping sickness with, David Bruce and leishmaniasis with Leishman. He was elected Fellow of the Royal Society in 1899 and awarded a knighthood, Knight Commander of the Order of St Michael and St George (KCMG) in 1903 and was appointed Knight Grand Cross of the Order of St Michael and St George (GCMG) in 1912. Manson never received the Nobel Prize that many of his peers felt that he richly deserved although he had been nominated, together with Laveran who was later awarded the Prize. Manson died in London in 1922.

For more information see Manson-Bahr, 1962; Chernin, 1983 and Stephens, 1937.

#### *Muriel Robertson 1883–1973*

Muriel Robertson was born in Glasgow and educated at the University of Glasgow where she graduated with an MA, specializing in Botany and Zoology, in 1905. She worked in the Zoology Department for 2 years and there she developed her interest in trypanosomes of fish. In 1907, as a recipient of the Carnegie Prize, she travelled to Ceylon to study the trypanosomes of reptiles and where she also continued to study the trypanosomes of fish. In 1910 she began working at the Lister Institute in London as assistant to the eminent protozoologist, Professor E. A. Minchin. In 1911 she was appointed protozoologist to what was then the Ugandan Protectorate. Robertson was greatly impressed by the work of Aldo Castellani, and partly due to his influence, worked in Uganda from 1911 to 1914 where she made a detailed study of the development of *Trypanosoma congolense* in several species of tsetse flies, *Glossina* spp., which she published in a series of important papers described in her obituary notice as ‘...classic in which the soundness of scientific observations was matched by the elegance of the illustration’, papers that are still relevant today. In 1913 she described the pleomorphic ‘long and thin’ and ‘short and stumpy’ forms of the trypanosomes in the blood and described how the latter were the forms infective to the tsetse flies. She also described the phenomenon of fluctuating parasitaemias in trypanosome infections and speculated that this phenomenon might have an immunological basis. While working in Uganda, Robertson developed a long lasting friendship and working relationship with David Bruce. Robertson’s work on trypanosomes was interrupted by the First World War when she worked on diseases caused by bacteria particularly gas gangrene and tetanus. She returned to London to work at the Lister Institute where she remained

for the rest of her working life first working with bacteria and later in 1941 with the protozoan *Trichomonas foetus*, an important cause of abortion in cattle and there she developed her interest in immunology. Her work was again interrupted by the Second World War when she resumed working on bacterial diseases. In 1947 Robertson was elected to a Fellowship of the Royal Society and retired from the Lister Institute in 1948 but continued to work until 1961 when she was nearly 80. She maintained an active interest in trypanosomes and noted with great pleasure the elaboration of her studies by younger workers using the newer techniques of cytochemistry and electron microscopy. She died in 1973 in Derry. For more information see Bishop and Miles, 1974; Clarke, 2004).

#### *Sir Ronald Ross 1857–1932*

Ronald Ross was born in Almora, present day Uttarakhand, in India to parents who were both born in India as were his grandparents who were descendants of the Earls of Ross an ancient Highland clan. Ross’s father wanted him to pursue a medical career and in 1874 he enrolled at St Bartholomew’s Hospital in London but left in 1880. In the meantime in 1879, he had passed the examinations for the Royal College of Surgeons and in 1881 became a licentiate of the Society of Apothecaries, a qualification that allowed him to join the Indian Medical Service. In 1883 he became interested in malaria and advocated limiting mosquito access to water as a means of controlling this disease. In 1894 he was on leave in London where he met Manson who persuaded him to investigate the possibility of the mosquito transmission of malaria. Ross was posted to Secunderabad in India and, after a number of false starts, observed, developmental stages of malaria parasites in anopheline mosquitoes. In 1897 his studies were interrupted when he was posted to Kherwara, where there was no malaria. Manson then intervened and ensured that he was posted to Calcutta (now Kolkata) where there were laboratory facilities that allowed him to demonstrate the complete life cycle of *Plasmodium relictum* in birds and culicine mosquitoes. In 1899, Ross joined the staff of the Liverpool School of Tropical Medicine where, in 1902, he became Professor and Chair of Tropical Medicine. While at Liverpool, Ross carried out important work on malaria, sleeping sickness, leishmaniasis and public health and established the field of epidemiology. In 1912 he was appointed Physician of Tropical Diseases at King’s College London, a position that he held concurrently with his post in Liverpool. During the First World War, Ross was an Honorary Consultant in Malariology to the British War Office and was later transferred to the Ministry of Pensions and

National Insurance. In 1926, with the establishment of the Ross Institute (later part of the London School of Hygiene and Tropical Medicine) in Putney, he became its first Director. Ross received many honours including, the Nobel Prize for Physiology or Medicine in 1902, Fellowship of the Royal Society in 1901, Companion of the Most Honourable Order of the Bath (KCB), in the same year, Knight Commander of the Order of St Michael and St George (KCMG) in 1918. Ross gradually became more and more cantankerous and was involved in a scurrilous debate with Battista Giovanni Grassi, who was part of the Italian team that demonstrated the mosquito transmission of malaria in 1898. Ross fell out with his students, colleagues and other scientists and even his onetime mentor, Patrick Manson.

For further information see Nye and Gibson, 1997 and Bynum, 2004.

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